

June 1, 1958 - May 31, 1959

## Progress Report for Research Grant H-1891 (C4)

During the current year, we have continued to collect basic data on successive classes of Johns Hopkins medical students, to pursue our follow-up studies, to make intensive investigations of certain aspects of our general studies and to analyze and report the results thus far obtained. Specifically, our activities may be summarized as follows:

## A. Collection of basic data.

1. In collaboration with the Personnel Health Clinic, admission physical examinations, urinalyses, teleoroentgenograms, serological tests for syphilis and serum cholesterol levels were all obtained on the entering class of 1962.
2. The class of 1962 is now coming into our laboratory by individual appointment for their initial studies. A battery of psychological tests, including a group Rorschach test, figure drawing test and Strong Vocational Interest Schedule is to be carried out on them this week.
3. Serum cholesterol levels were measured this fall on members of the class of 1961, just a year after their entrance to medical school.
4. Members of the class of 1961 have come in by individual appointment for ballistocardiographic smoking tests; these are nearly complete.
5. The class of 1959 has been instructed how to obtain detailed information for the "long form" family history questionnaire in collaboration with parents and home physician. When this is complete, the subject comes in for final interview by appointment. At that time, another cholesterol level is obtained as well as blood pressure, heart rate and body weight.

## B. Follow-up studies.

1. The five year follow-up is being carried out on the class of 1954 by means of a questionnaire.
2. The ten year follow-up is being carried out in similar fashion on the class of 1949, the second class thus studied.

## C. Special investigations.

1. Further studies on the effect of Vitamin B<sub>12</sub> on cholesterol level are in progress to check our preliminary findings of last year which appeared to show that Vitamin B<sub>12</sub> administered orally lowers cholesterol levels in healthy young adults. A double blind experiment is being carried out on eight pairs of

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subjects from the class of 1961 matched as to cholesterol level and on one additional hypercholesteremic subject. Four control cholesterol determinations based on duplicate serum samples and an equal number of blood Vitamin B<sub>12</sub> determinations were obtained on each subject in December and January. During February and March, one member of each pair received Vitamin B<sub>12</sub> orally in the form of "Visorbin", while the other member received a placebo. During April and May, the group first given Vitamin B<sub>12</sub> is receiving the placebo, while the original group is now on Vitamin B<sub>12</sub>. Both substances are supplied us through the kindness of Smith, Kline and French. The Vitamin B<sub>12</sub> determinations are carried out without charge in Dr. Bacon Chow's laboratory. Cholesterol levels and blood Vitamin B<sub>12</sub> levels are obtained weekly.

2. Because our studies of the medical students raised the possibility of seasonal variation of cholesterol levels, we are studying the effect of time of year on the cholesterol level of a group of healthy young adults in Baltimore who presumably live under more uniform conditions than the medical students as to periods of stress (examinations) on the one hand, and relaxation (vacations) on the other. The subjects for this study are 25 white male prisoners aged 20-29 years in the Maryland Penitentiary, which is less than a mile from the medical school. Monthly cholesterol determinations on each subject were begun in the fall and will continue for a year. All of the prisoners selected had been confined for more than a year at the start of the experiment and none were scheduled to be released within a year of it's termination.
3. This year we have made a systematic, detailed classification of the pairs of figure drawings produced by over 750 medical students as part of our psychological testing program. To our knowledge, no such classification has been described by others.
4. Under a grant from the Tobacco Industry Research Committee, we are comparing the figure drawings of smokers versus nonsmokers by this method. A preliminary comparison of the drawings of 24 smokers and 24 nonsmokers was made blind by Dr. Irvin Greenberg. Where differences were found, the drawings of 48 additional subjects, also equally divided as to being smokers or nonsmokers, were examined.
5. We are making further observations to answer the question: do smokers and nonsmokers have genetic differences? A survey of healthy blood donors (excluding medical students) is in progress, supported by the Tobacco Industry Research Committee. This study is to serve as an independent check of our previously reported findings based on studies of the medical students:
  - a. that a greater proportion of smokers than nonsmokers have high cholesterol levels.
  - b. that smokers more frequently have a positive parental history of hypertension and/or coronary heart disease than do nonsmokers.

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Dr. Bernice Cohen, an expert in the field of human genetics, is associated with me in this study. Blood donors are interviewed concerning smoking habits and parental history of hypertension and/or coronary heart disease. The Rh and ABO blood groupings as determined at the Johns Hopkins Blood Bank are recorded, and the donors are classified as "tasters" or "nontasters" of phenylthiocarbamide, a genetic marker. A cholesterol level is obtained on white male donors only for comparison with our findings on white male medical students.

D. Analysis of collected data.

1. We have continued to transfer the data for the classes of 1948-1958 to IBM punch cards. So far, eleven such cards per individual have been completed which include the following data: identification and general information; family history; medical history; blood pressure and heart rate under different circumstances; cholesterol levels; ballistocardiographic smoking test; smoking habits and four-way grouping; habits of nervous tension; Rorschach test; high lights of habit survey; sodium withdrawal studies and eosinophil counts. In the process of completion are cards concerned with the oximeter-controlled anoxemia test; figure drawings; life tables for parents of subjects.
2. In December, 1958, we were fortunate in receiving a supplementary grant from the National Heart Institute to cover the salary of a full-time statistician for two years to collaborate with the director of the study in writing a monograph on the collected data. With the help of Dr. Abraham Lillienfeld, Professor and Head of the Division of Chronic Disease in the School of Hygiene and Public Health, we have conducted an intensive search to find a well-qualified person. Several candidates have been interviewed and we hope to fill the position shortly.

E. Reporting of results.

1. Three talks based on our findings have been given:
  - a. On October 24, 1958, a paper entitled "Familial Patterns in Hypertension and Coronary Heart Disease" was presented as part of a symposium on genetic factors in cardiovascular disease at the 31st Scientific Sessions of the American Heart Association in San Francisco, California.
  - b. On November 21, 1958, a paper entitled "Hypertension and Humanity" was presented at the Annual Fall Conference of the Council for High Blood Pressure Research of the American Heart Association in Cleveland, Ohio.
  - c. On February 18, 1959, a discussion of our studies on the precursors of hypertension and coronary disease

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was presented at a staff seminar at the Howard University School of Medicine in Washington, D.C.

2. Three papers have been published:

- a. Thomas, C.B. and Murphy, E.A.: The Circulatory Response to Smoking. J. Chr. Dis. 8:202, 1958.
- b. Thomas, C.B. and Murphy, E.A.: Further Studies on Cholesterol Levels in the Johns Hopkins Medical Students: The Effect of Stress at Examinations. J. Chr. Dis. 8:661, 1958.
- c. Thomas, C.B.: Cholesterol Characteristics. Maryland State Med. J., 8:2, 1959.

3. Two papers are in press and will appear shortly:

- a. Thomas, C.B. and Murphy, E.A.: Observations on Some Possible Precursors of Essential Hypertension and Coronary Artery Disease: VI. Comparison of the Circulatory Reactivity to the Cold Pressor Test and to the Smoking Test, to appear in Ann. Int. Med., Apr., 1959.
- b. Thomas, C.B.: Familial Patterns in Hypertension and Coronary Heart Disease, to appear in Circulation, May, 1959.

4. One paper has recently been submitted for publication:

- a. Thomas, C.B. and Eisenberg, F.F.: Variability of Cholesterol Levels in Individual Johns Hopkins Medical Students, with Observations on Stopping Smoking, Vitamin B<sub>12</sub> Administration and Acute Infection.

5. Three papers are in the process of completion:

- a. Thomas, C.B. Comparison of Healthy Young Smokers and Nonsmokers as to Parental History and Individual Characteristics.
- b. Thomas, C.B. and Murphy, E.A.: The Effect of Minimal Doses of Hexamethonium Chloride and Wyamine Sulphate on the Circulatory Response to Smoking.
- c. Garn, S.M. and Thomas, C.B.: Degree of Obesity and Serum Cholesterol Level.

6. An application has been made to the Heart Association of Maryland for funds to support the republication in a single volume of the first twenty-five papers arising from this study (including those listed under 2 and 3 above).

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